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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,128	12/07/2001	John Carrino	INVIT1290-2	1163

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EXAMINER
CALAMITA, HEATHER

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,128	CARRINO ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/30/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. In response to amendment, the objection to the specification is withdrawn. The cancellation of claims 57-74 and the amendment to claims 1, 15 and 25 are acknowledged. However, all 102(b) and 103(a) rejections are hereby maintained.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5,8-10,12-14,25,26,28-31,37-41, 44,45, 49-54 are rejected under 35U.S.C. l02(b) as being anticipated by Shuman et al. (USPN 5,766,891 June 16, 1998).

Shuman teach a method of generating a double stranded recombinant nucleic acid comprising contacting a first ds nucleotide derived from subpopulation and a second ds nucleotide sequence and at least one topoisomerase such that topoisomerase covalently link both strands of first sequence to second sequence generating a ds recombinant molecule (see whole doc. esp. abstract & col. 6 line 21). In particular they teach PCR amplifying a donor duplex DNA molecule with oligonucleotide primers containing sequence specific topoisomerase cleavage site, incubating the donor duplex DNA with a sequence specific topoisomerase, resulting in the formation of a sequence specific topoisoemrase donor duplex DNA incubating with plasmid vector with 5 overhand compatible with donor and incubating and transforming vector into host cell (see col. 6 line 60- col. 7 line 6). They teach that the transforming host cell with DNA sequence to encoding a polypeptide activity (see abstract). They teach using vaccinia DNA topoisomerase which is type 1 topoisomerase (see col. l line 25-26). They teach regulatory elements including promoter and

enhancer to bind RNA polymerase. They lac promoter, start codon and termination codon (see col. 7 line 27-40). They also teach poly histidine tags (see col. 5 line 34). They teach using affinity labels such as biotin introduced into the DNA product to purify the product (see col. 6 line 21-26).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. l03(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR l .56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. l03(c) and potential 35 U.S.C. 102(e), (9 or (g) prior art under 35 U.S.C. l03(a).

Claims 32-34,36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuman (USPN 5,766,891 June 16, 1998).

The teachings of Shuman et al. are described previously.

Shuman et al. do not teach using a third ds sequence.

One of ordinary skill in the art would have been motivated to further bind a third sequence in order to build a desired construct. It was well known in the art to build long constructs from smaller fragments. It would have been prima facie obvious to further construct longer ds sequences by covalently bonding with Shuman's topoisomerase to build longer

sequences for insertion into vectors.

5. Claims 6,7, 11, 15-24,27,35 are rejected under 35 U.S.C. l03(a) as being unpatentable over Shuman et al. (USPN 5,766,891 June 16, 1998) in view of Yarovinsky et al. (US2002/0068290 June 6, 2002).

The teachings of Shuman et al. are described previously.

Shuman et al. do not teach poxvirus vaccinia, topoisomerase charged adapters.

Yarovinksy et al. teach topoisomerase activated oligonucleotide adapters for covalently bonding sequences (see whole doc. esp. abstract & paragraph 0010). They teach poxvirus (paragraph 0062). They teach joining various targets particularly using Shuman et al's technique (see paragraph 004).

One of ordinary skill in the art would have been motivated to apply Yarovinksy's topoisomerase activated oligonucleotides to Shuman's method of covalent linkage in order to bind the amplified sequences into vectors. Yarovinsky et al. state that topoisomerase activated oligonucleotides provide for rapid joining of target to adaptor sequences (see paragraph 005). It would have been prima facie obvious to apply Yarovinksy's adaptors to Shuman's method in order to quickly join amplified sequences into vectors.

6. Claims 42 & 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuman et al. (USPN 5,766,891 June 16, 1998) in view of Seed et al. (USPN 5,830,731 Nov. 3, 1998).

The teachings of Shuman et al. are described previously.

Shuman et al. do not teach expression of -1-7 suppressor.

Seed et al. teach 7-7 suppressor gene in expression vector (see col. 6 line 24).

One of ordinary skill in the art would have been motivated to apply Shuman's method of construction to expression Seed's T7 suppressor gene in order to express and

produce T7 suppressor. Seed et al. state that the T7 suppressor may be used in diagnostic and therapeutic purposes (see abstract). It would have been prima facie obvious to use Shuman's cloning procedure in order to quickly express and produce Seed's -1-7 suppressor gene.

7. Claims 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuman et al. (USPN 5,766,891 June 16, 1998) in view of Trono et al. (USPN 5,605,802 Feb. 25, 1997).

The teachings of Shuman et al. are described previously.

Shuman et al. do not teach histidine tag attached to DNA sequences.

Trono et al. teach histidine tags in expression vectors (see col. 1 2 line 17).

One of ordinary skill in the art would have been motivated to apply Trono's teaching of histidine tags to Shuman's expression system in order to purify the expressed protein. It was well known and commonly practiced in the art to fuse histidine tags to genes in vectors to aid in affinity purification. It would have been prima facie obvious to apply Trono's histidine tags to the expressed proteins in Shuman's system in order to quickly purify the protein to isolation.

Response to Arguments

8. Applicant's arguments filed June 30, 2004 have been fully considered but they are not persuasive.

The 102 rejections directly address the amended claims, and are therefore maintained.

The 103 rejections directly address the amended claims and are therefore maintained.

Applicant states Shuman describes methods for linking duplex DNA molecules using topoisomerase. Applicant further states Shuman depicts a first ds nucleotide sequence having a topoisomerase bound to each 3' terminus ("topoisomerase charged bivalent linker"), and a second

ds nucleotide sequence comprising a linearized vector (Hind III cleaved pUC18). Upon contact of the first and second ds nucleotide sequences shown in Figure 5, the 3' termini of the first ds nucleotide sequence (shown with the "T" topoisomerase) will be covalently linked to the 5' termini of the second ds nucleotide sequence (see, also, col. 7, lines 13-27). As such, the first ds nucleotide sequence is linked to the vector in one strand at each end, but not in the second strand of each end.

Applicant asserts the present claims require the topoisomerase covalently link both strands of at least one end of the first ds nucleotide sequence to both strands of at least one end of the second ds nucleotide sequence to obtain a recombinant ds nucleic acid molecule that "does not contain a nick in either strand at the position where the ds nucleotide sequences are joined."

In response to applicant's argument, the examiner points out that Shuman teaches transforming *E. coli* cells with the plasmid vector containing the insert (see Figure 5A). Transformation into *E. coli* would eliminate the nick in the second strand at each end of the ds nucleotide sequence as a result of the bacterial ligase present. Applicant uses the open language of comprising in the claims allowing for the additional step of transformation. Therefore, Shuman meets applicant's aforementioned requirement of a ds recombinant nucleic acid molecule that does not contain a nick in either strand at the position where the ds nucleotide sequences are joined.

9. Applicant argues, in all of the 103(a) rejections, the examiner's conclusion of obviousness is based upon the improper application of Shuman's teachings. Applicant's arguments with respect to these rejections have been considered but are moot in view of the clarification of Shuman's teachings.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita, Ph.D. whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday thru Thursday 7:00 A.M. - 5:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571.272.0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

hgc

JEFFREY FREDMAN
PRIMARY EXAMINER
8/9/04